

Fig.1

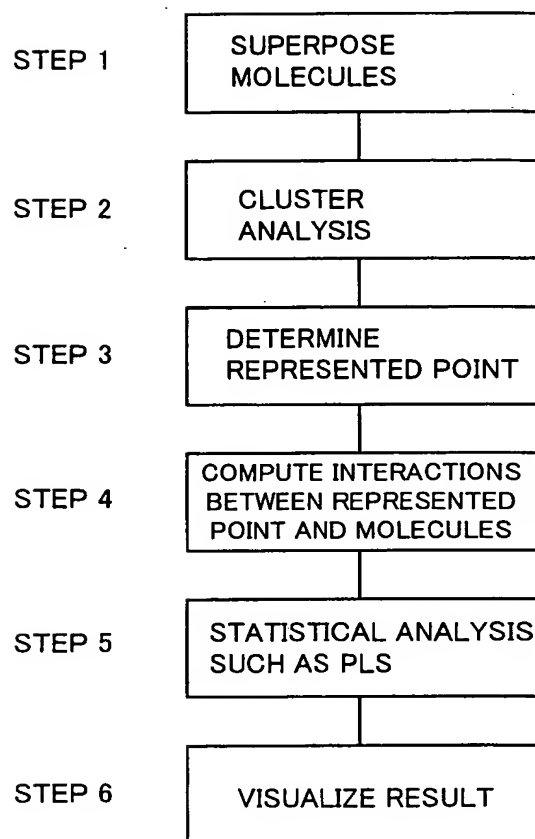


Fig.2A

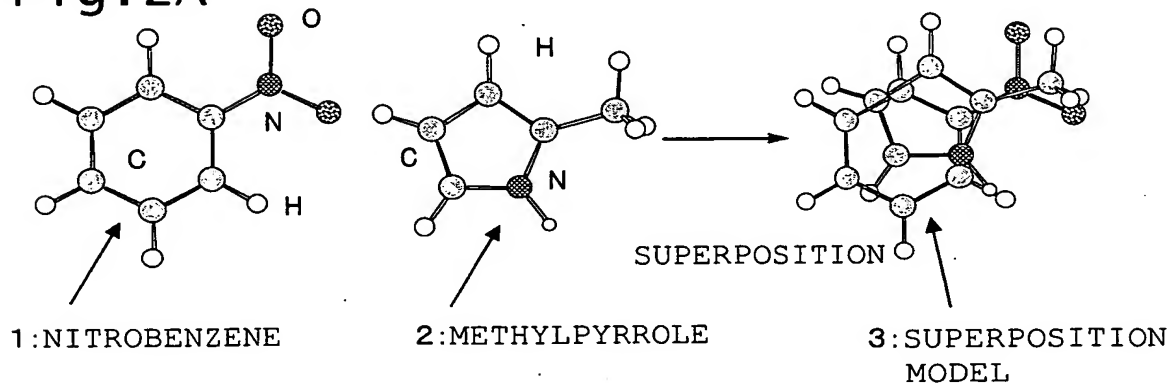


Fig.2B

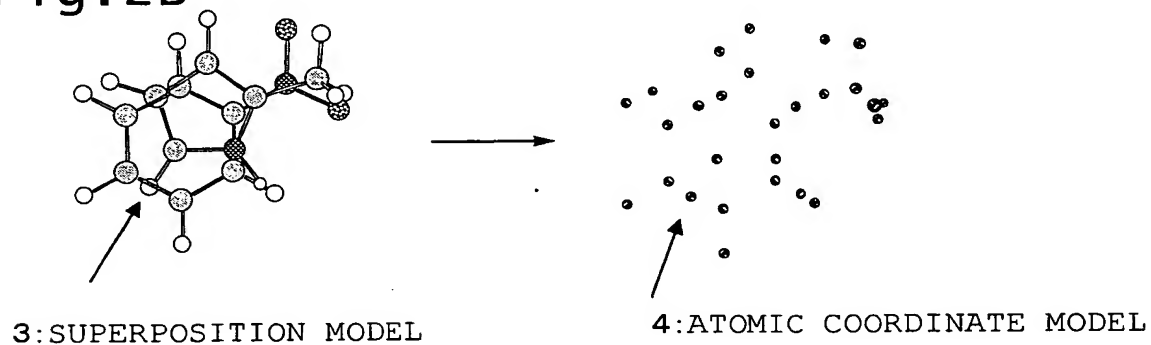


Fig.2C

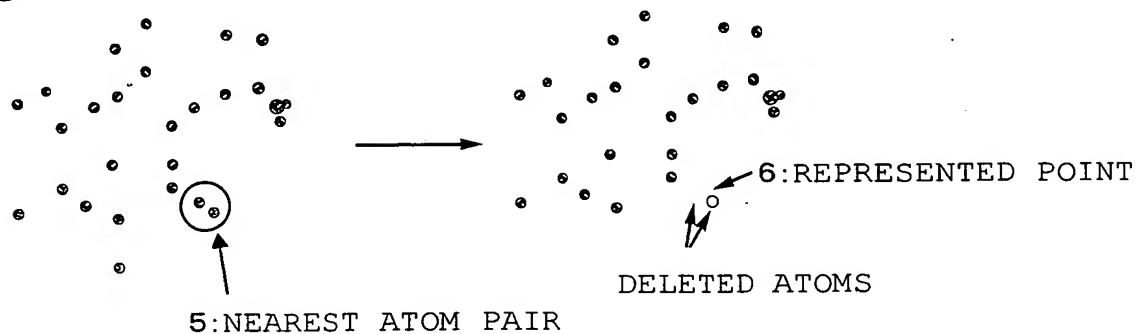


Fig.2D

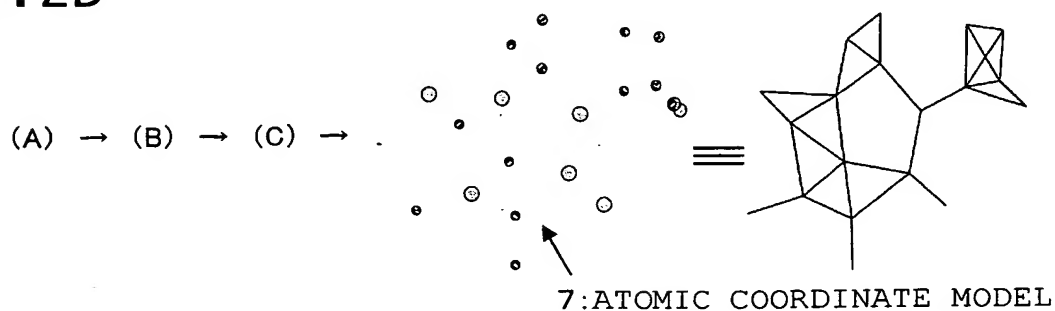
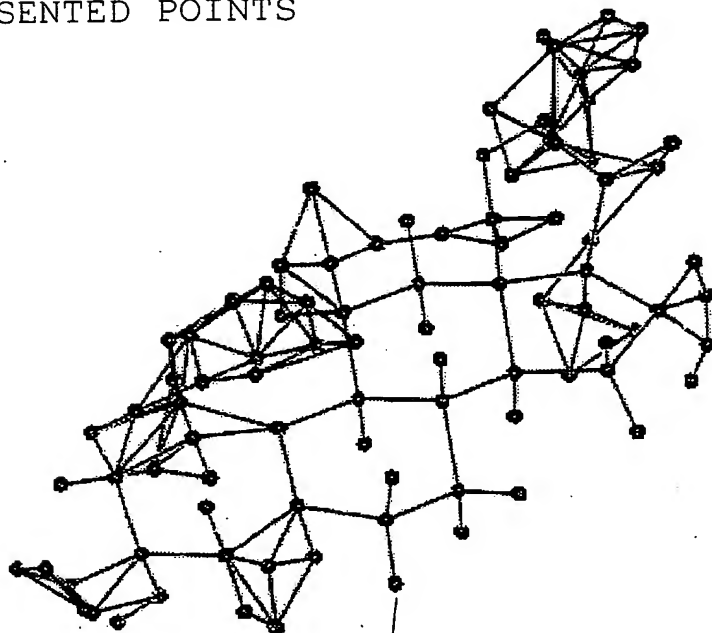


Fig.3

REPRESENTED POINTS



SPREAD SHEET

	Acti- vity	S01	S02	S03 ... S50	E01 ... E50
COMPOUND 1	5.1				
COMPOUND 2	6.8				
...					
...					
...					
...					
COMPOUND20					

PLS

STRUCTURE-ACTIVITY RELATIONSHIP FORMULA

$$\text{ACTIVITY} = y + a \times S01 + b \times S02 + \dots + z \times E50$$

## Fig. 4

## COMPOUND SET USED FOR VERIFICATION OF 3D QSAR

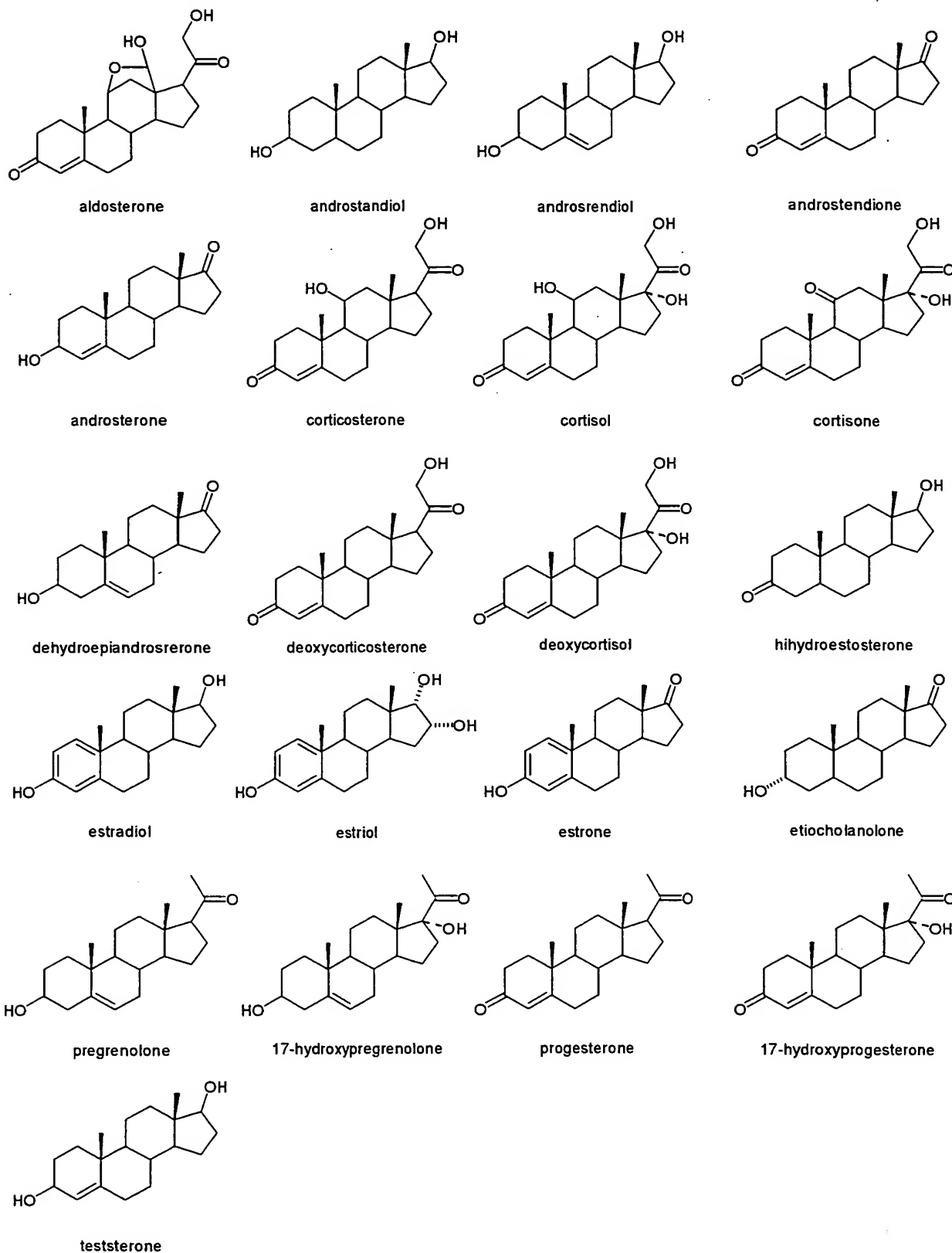
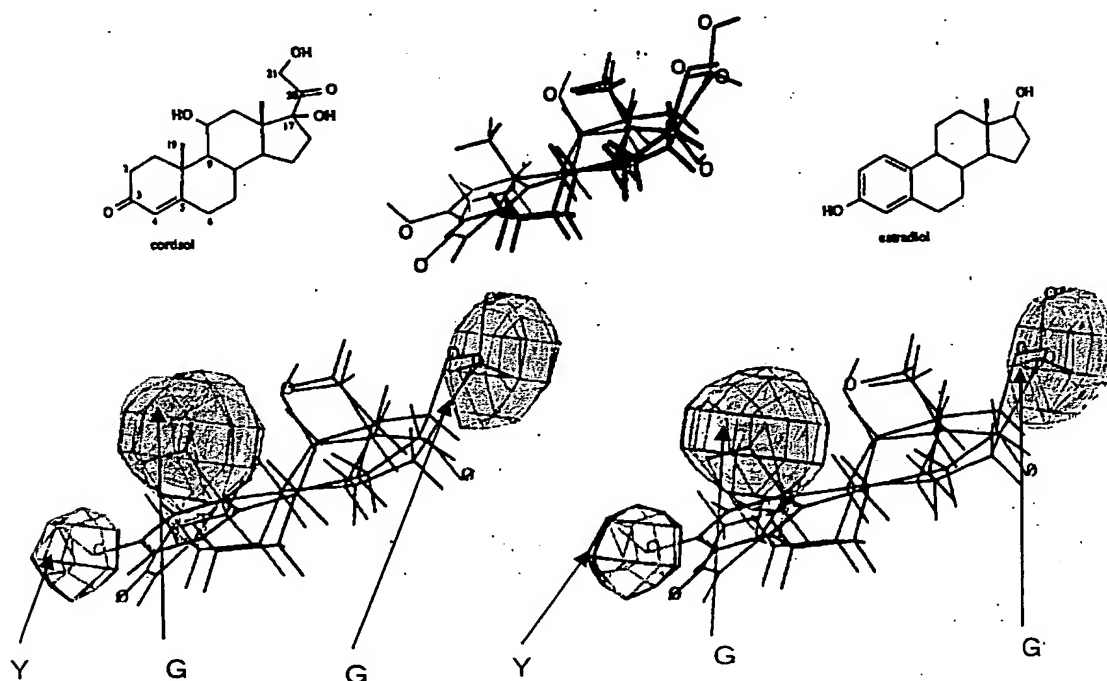


Fig.5

## ISOCONTOUR MAPS OF STERIC CONTRIBUTIONS IN CoMSIA

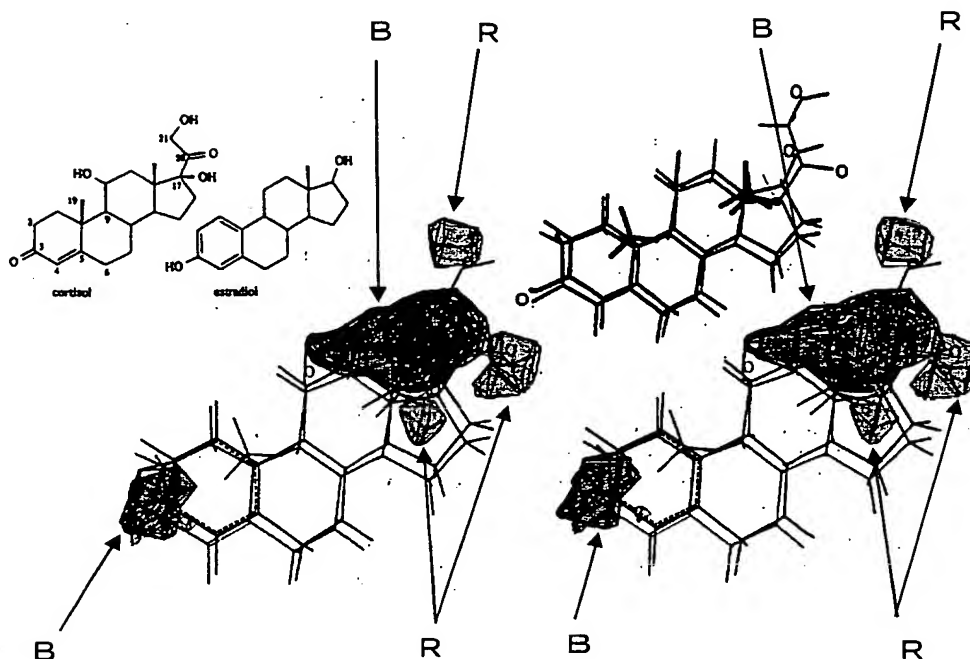


G: REGIONS WHERE ACTIVITY WILL BE ENHANCED  
STERICALLY

Y: REGIONS WHERE ACTIVITY WILL BE WEAKENED  
STERICALLY

Fig.6

## ISOCONTOUR MAPS OF ELECTROSTATIC CONTRIBUTIONS IN CoMSIA



THICK LINES: REGIONS WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
THIN LINES: REGIONS WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
B: REGIONS WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
R: REGIONS WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY

Fig.7

REPRESENTED POINTS ARE GENERATED BASED ON  
ATOMIC COORDINATES OF SUPERPOSED MOLECULES  
(POINTS OF INTERSECTION ARE REPRESENTED POINTS)

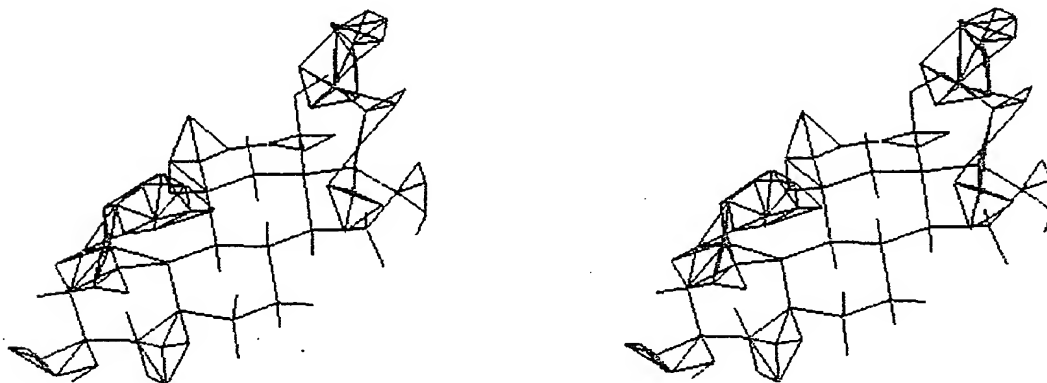


Fig.8

REPRESENTED POINTS ARE GENERATED,  
ADDING NEW POINTS IN CENTRAL PORTION OF RING

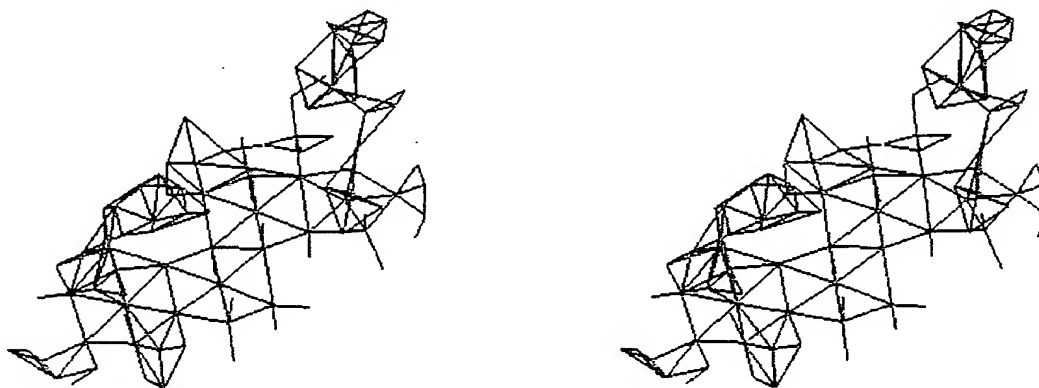
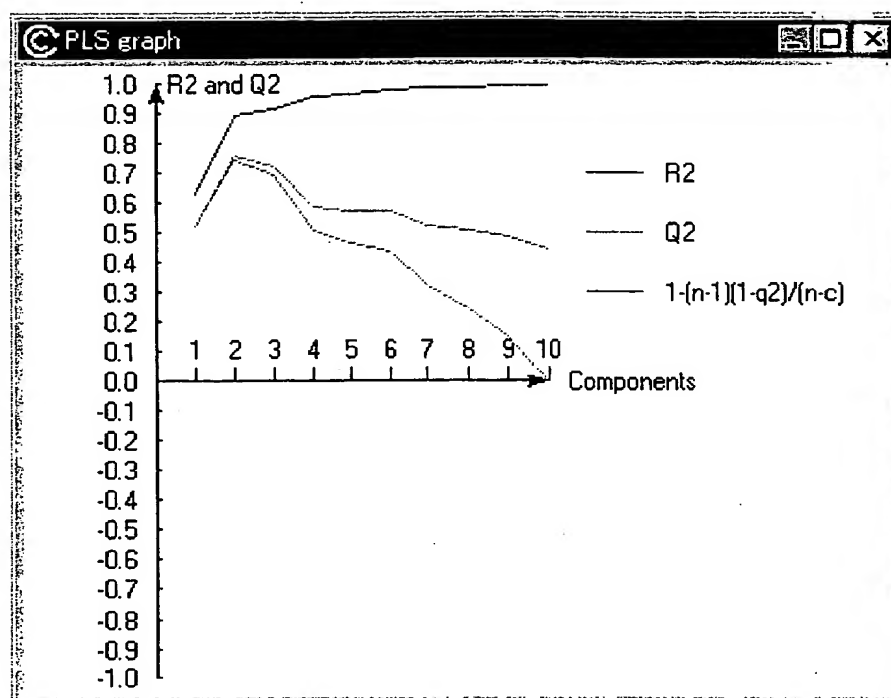


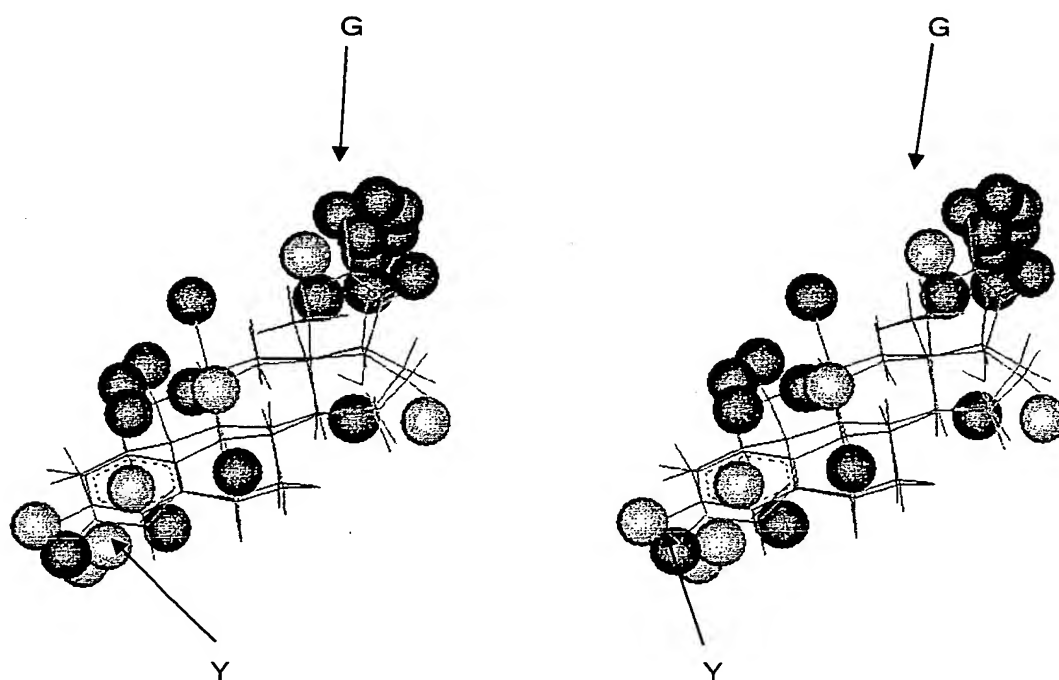


Fig.9



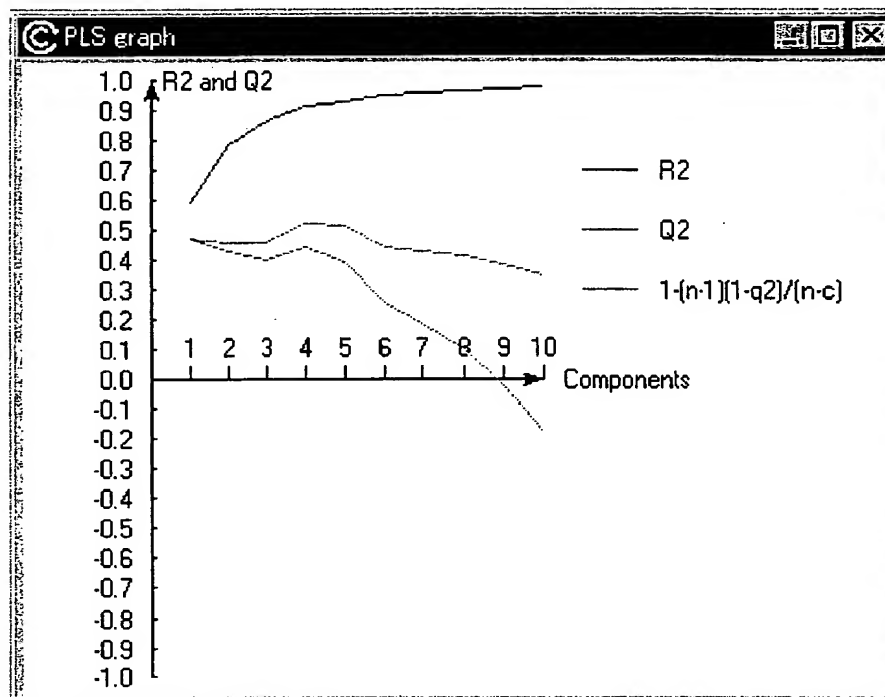
Components 2  
R2: 0.899  
Q2: 0.760

Fig.10



G: REGIONS WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
 Y: REGIONS WHERE ACTIVITY WILL BE WEAKENED  
 (REGIONS WHERE COEFFICIENT  
 IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.1 OR MORE)

Fig.11



Components 4

R2: 0.915

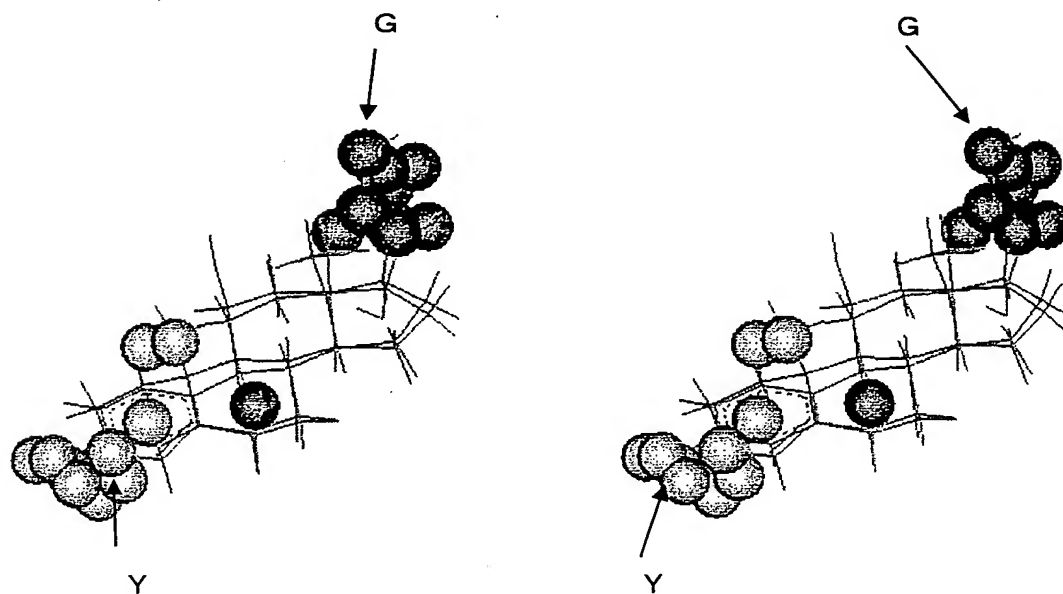
Q2: 0.528

Electrostatic :0.757

Steric :0.243

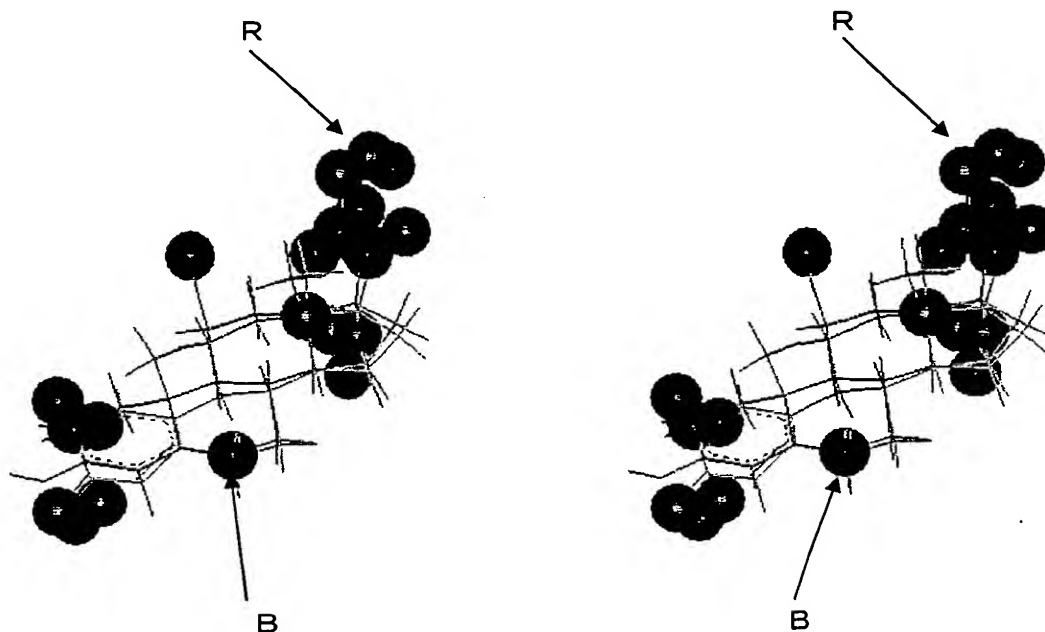
12/50

Fig.12



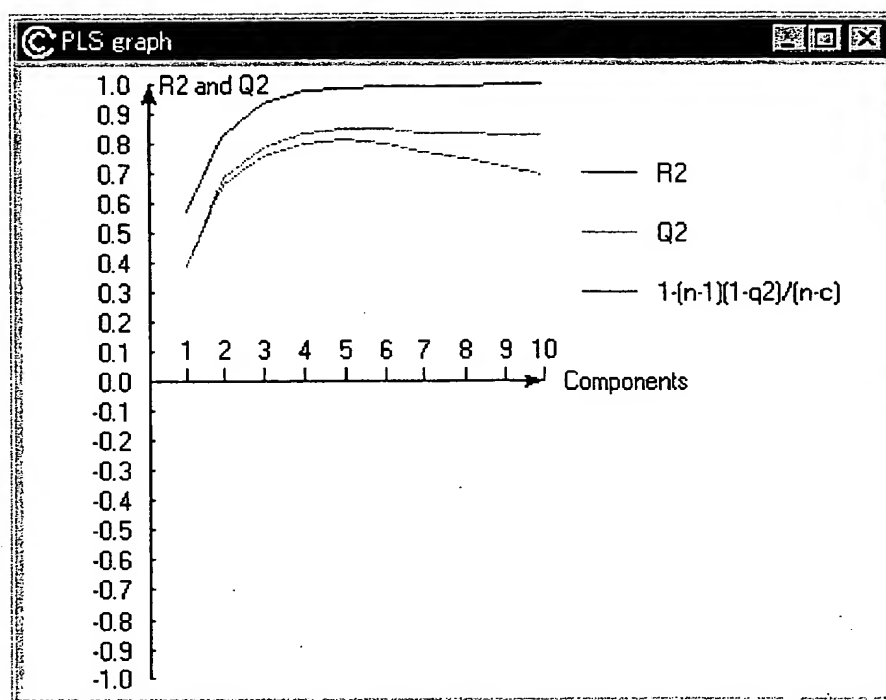
G: REGIONS WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
Y: REGIONS WHERE ACTIVITY WILL BE WEAKENED  
(REGIONS WHERE COEFFICIENT  
IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.1 OR MORE)

Fig.13



B: REGIONS WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
R: REGIONS WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
(REGIONS WHERE COEFFICIENT  
IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.2 OR MORE)

Fig.14



Components 4

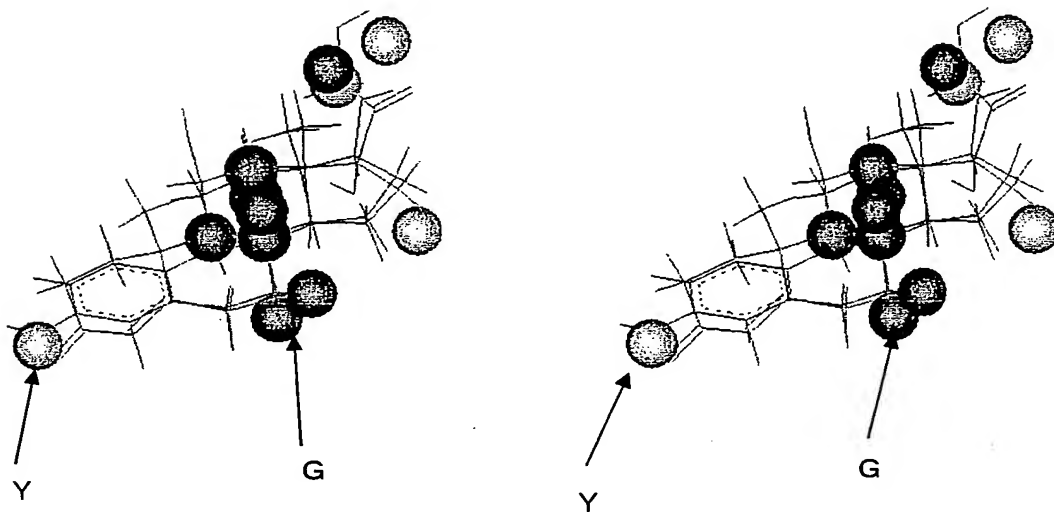
R2: 0.984

Q2: 0.822

Electrostatic :0.458

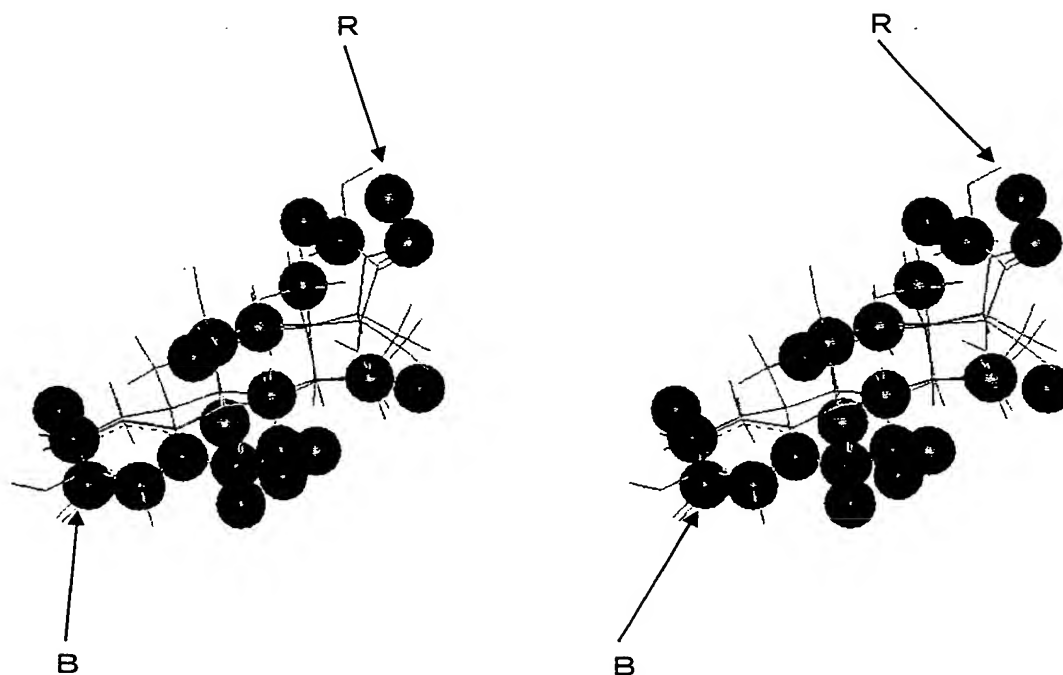
Steric :0.542

Fig.15



G: REGIONS WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
Y: REGIONS WHERE ACTIVITY WILL BE WEAKENED  
(REGIONS WHERE COEFFICIENT  
IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.2 OR MORE)

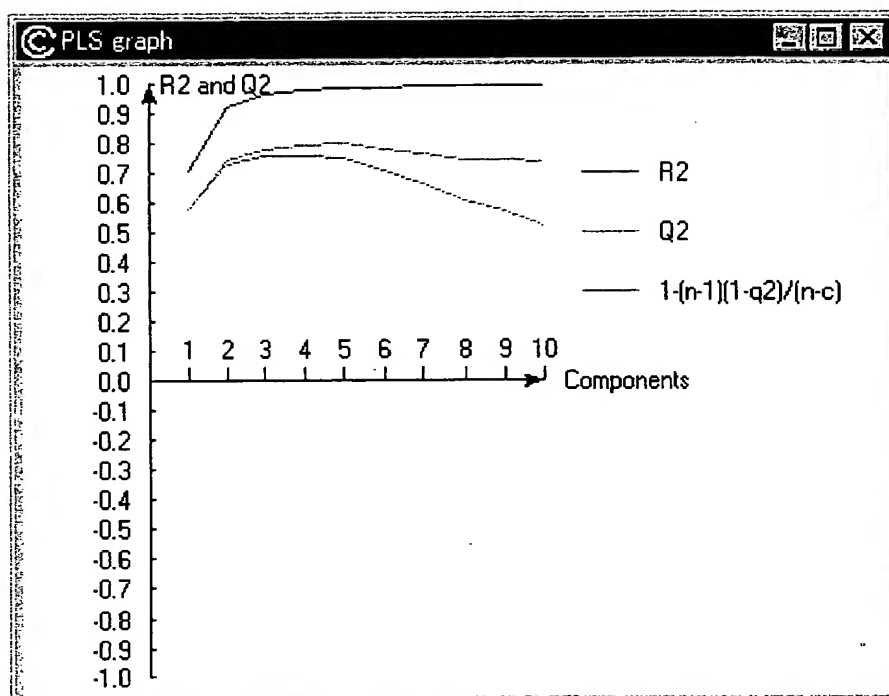
Fig.16



B: REGIONS WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
 R: REGIONS WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
 (REGIONS WHERE COEFFICIENT  
 IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.2 OR MORE)

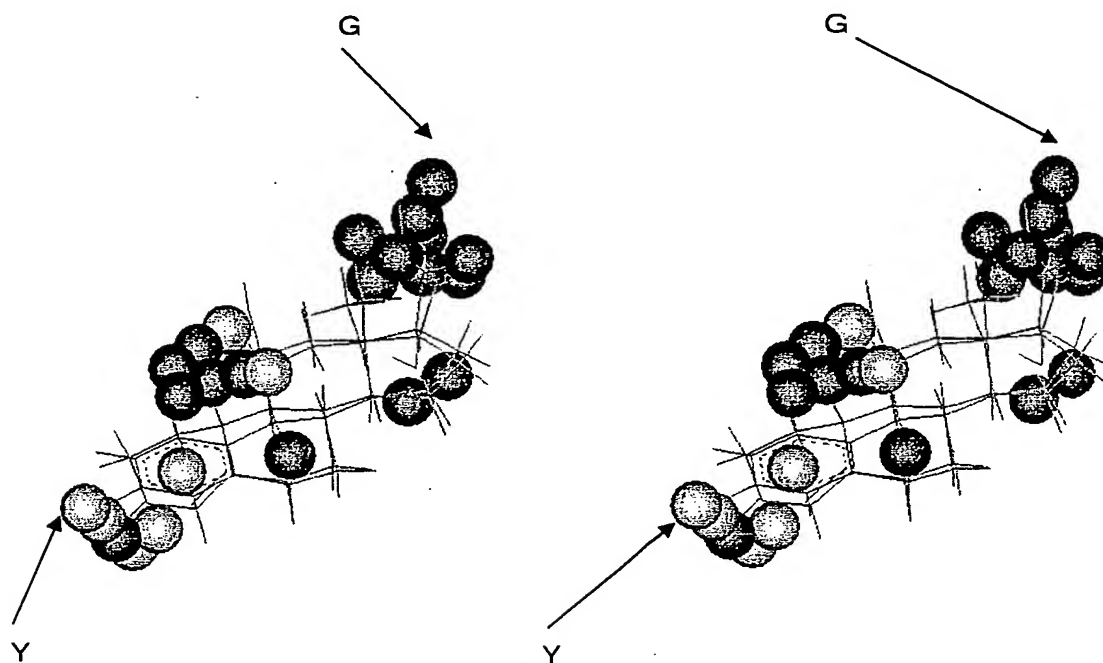


Fig.17



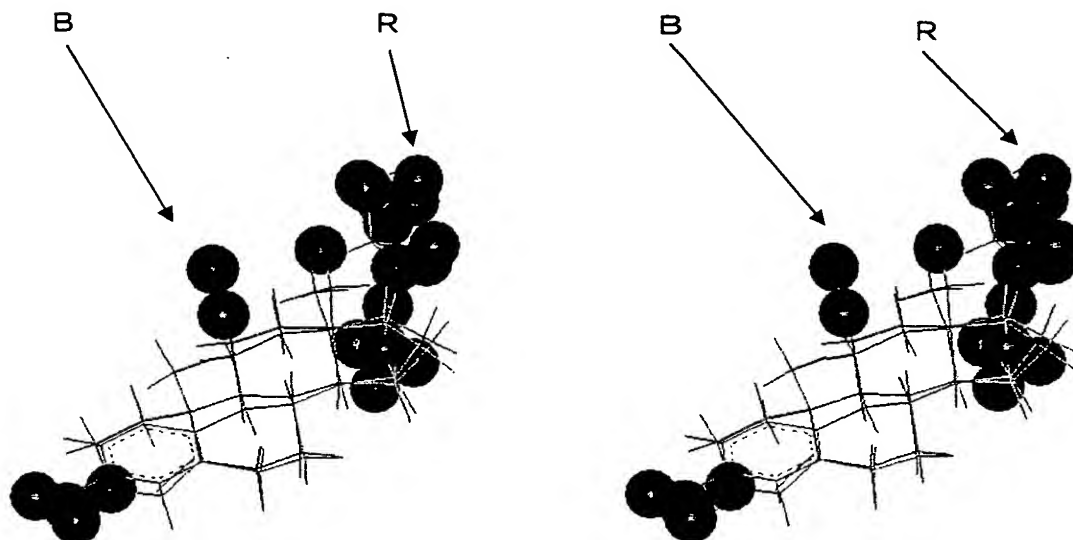
Components 4  
R2: 0.982  
Q2: 0.798  
Electrostatic :0.500  
Steric :0.500

Fig.18



G: REGIONS WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
Y: REGIONS WHERE ACTIVITY WILL BE WEAKENED  
(REGIONS WHERE COEFFICIENT  
IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.15 OR MORE)

Fig.19

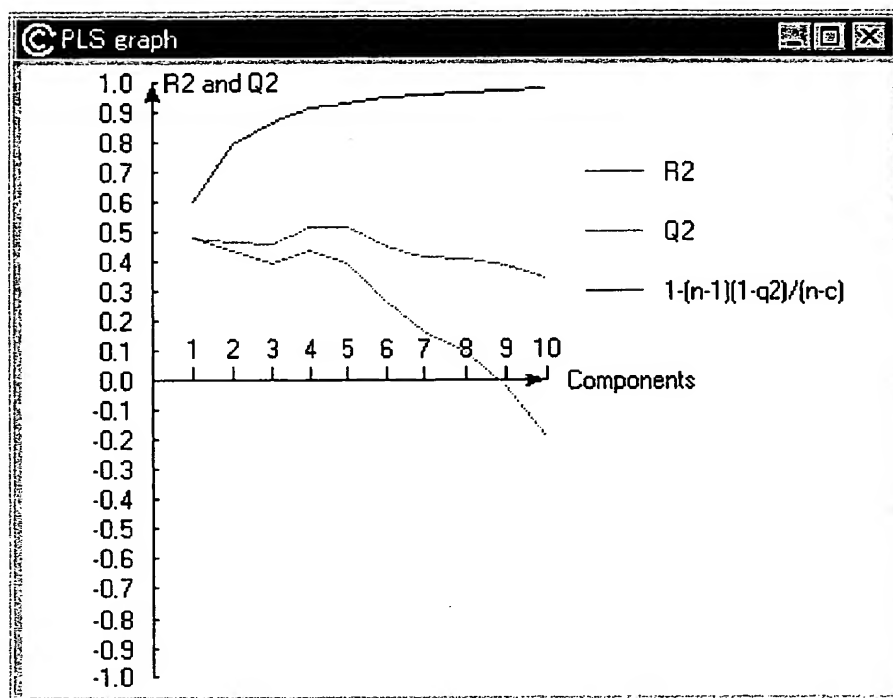


B: REGIONS WHERE POSITIVE CHARGES WILL ENHANCE  
ACTIVITY

R: REGIONS WHERE NEGATIVE CHARGES WILL ENHANCE  
ACTIVITY

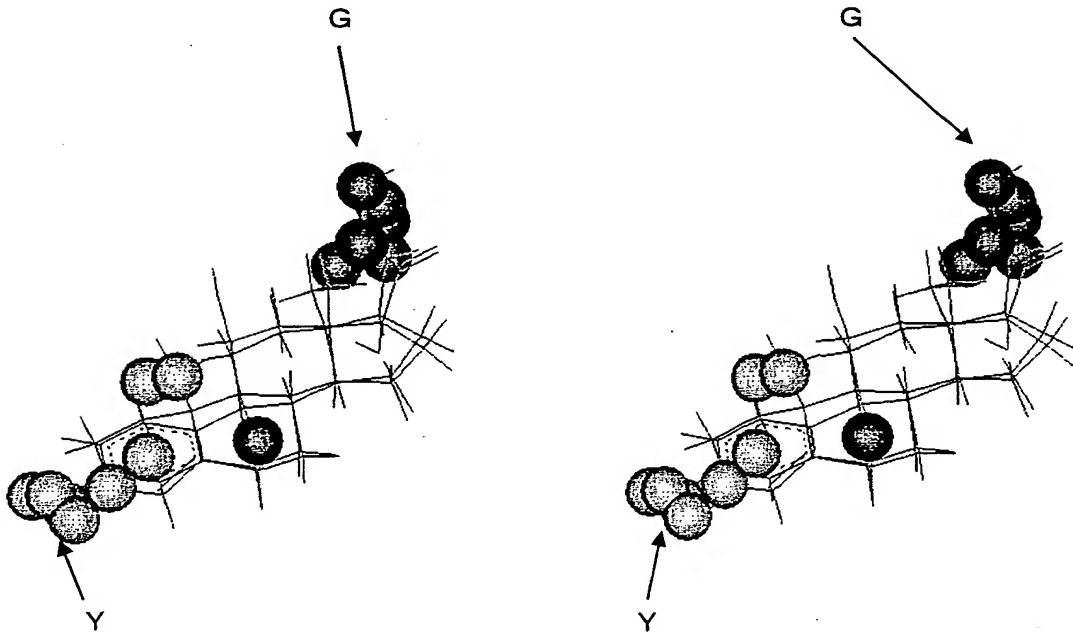
(REGIONS WHERE COEFFICIENT  
IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.2 OR MORE)

Fig.20



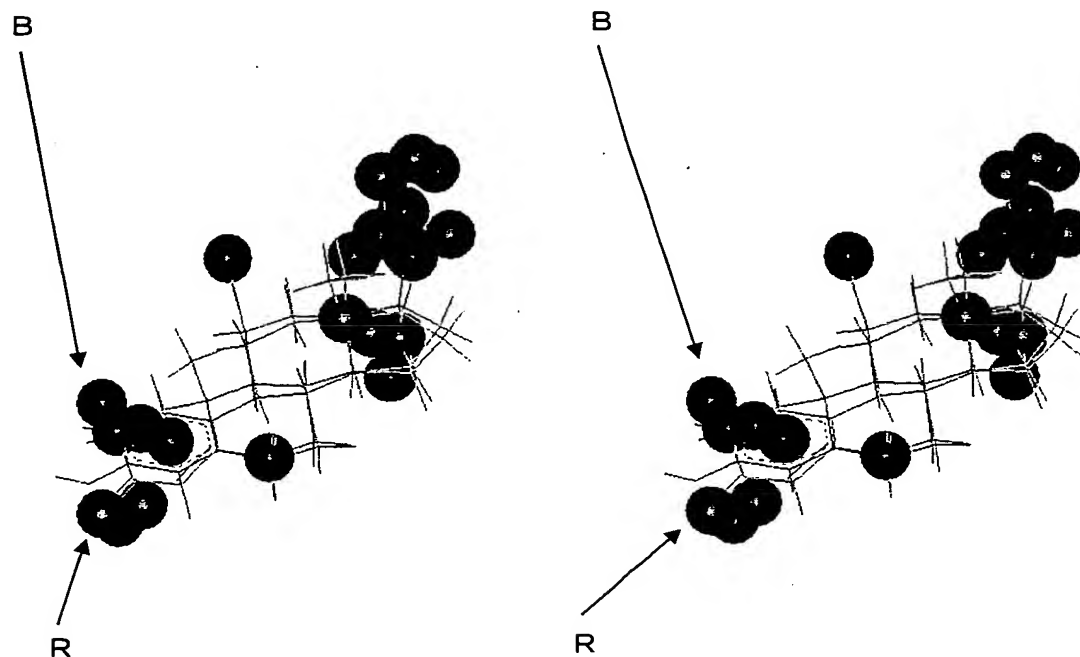
Components 4  
R2: 0.915  
Q2: 0.521  
Electrostatic :0.783  
Steric :0.217

Fig.21



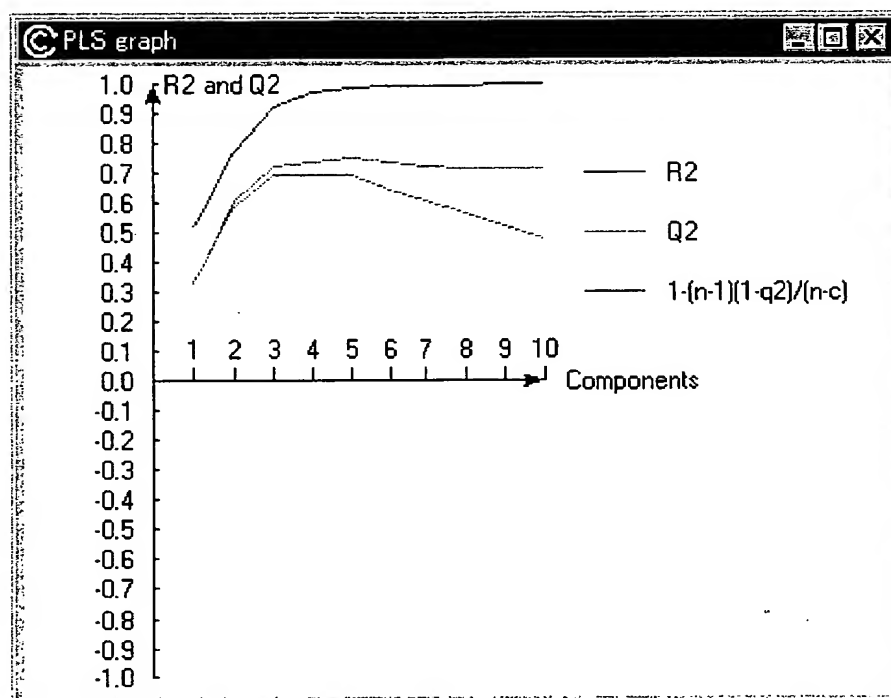
G: REGIONS WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
Y: REGIONS WHERE ACTIVITY WILL BE WEAKENED  
(REGIONS WHERE COEFFICIENT  
IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.1 OR MORE)

Fig.22



B: REGIONS WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
R: REGIONS WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
(REGIONS WHERE COEFFICIENT  
IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.3 OR MORE)

Fig.23



Components 4

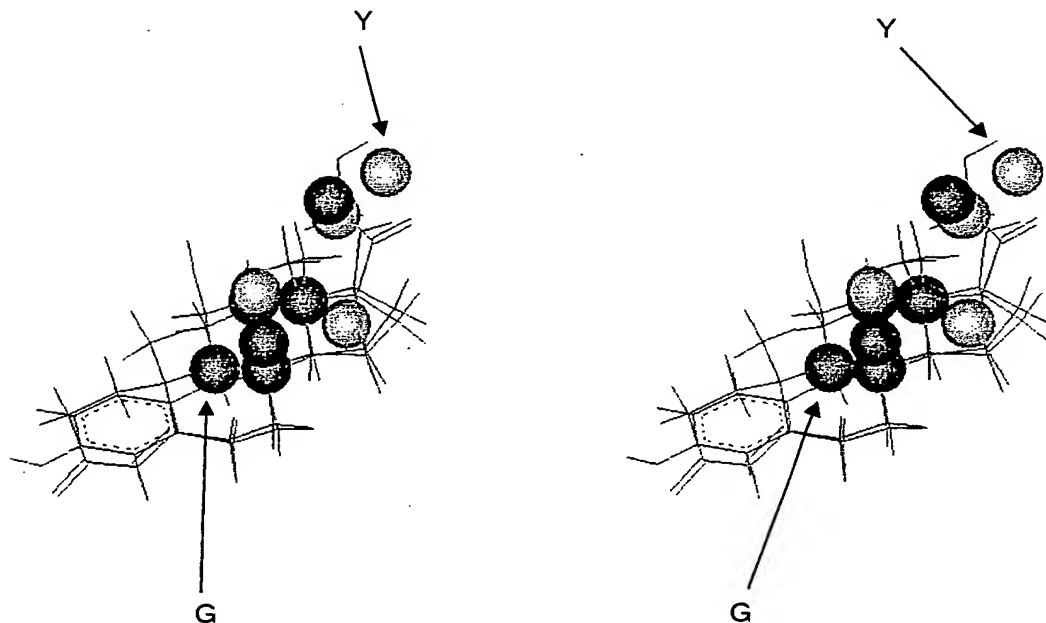
R2: 0.976

Q2: 0.741

Electrostatic :0.480

Steric :0.520

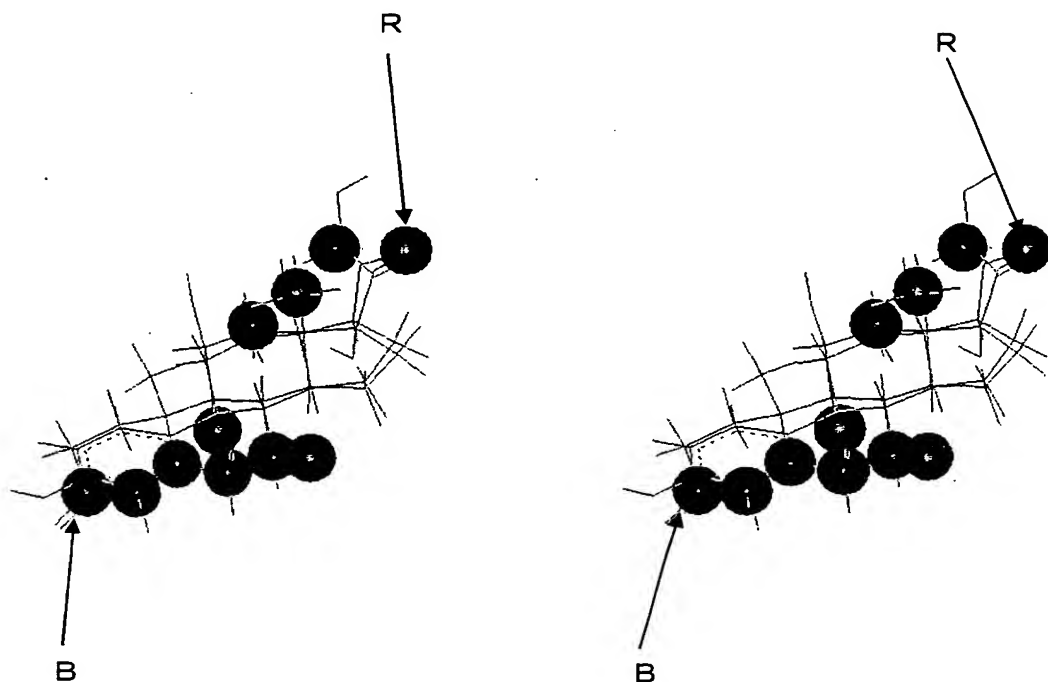
Fig.24



G: REGIONS WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
Y: REGIONS WHERE ACTIVITY WILL BE WEAKENED  
(REGIONS WHERE COEFFICIENT  
IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.3 OR MORE)

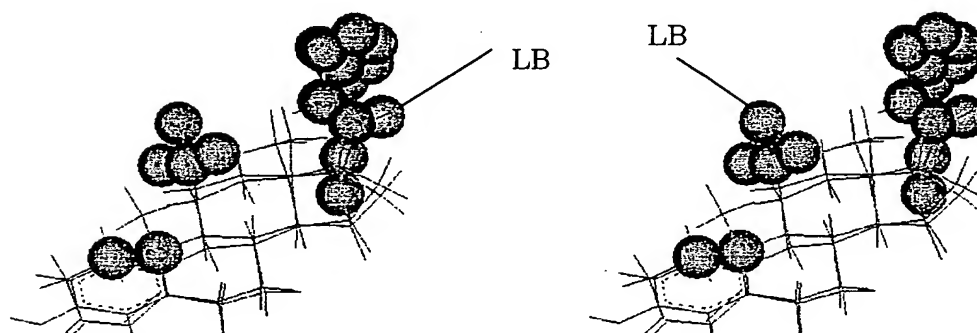


Fig.25



B: REGIONS WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
R: REGIONS WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
(REGIONS WHERE COEFFICIENT  
IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.3 OR MORE)

Fig.26

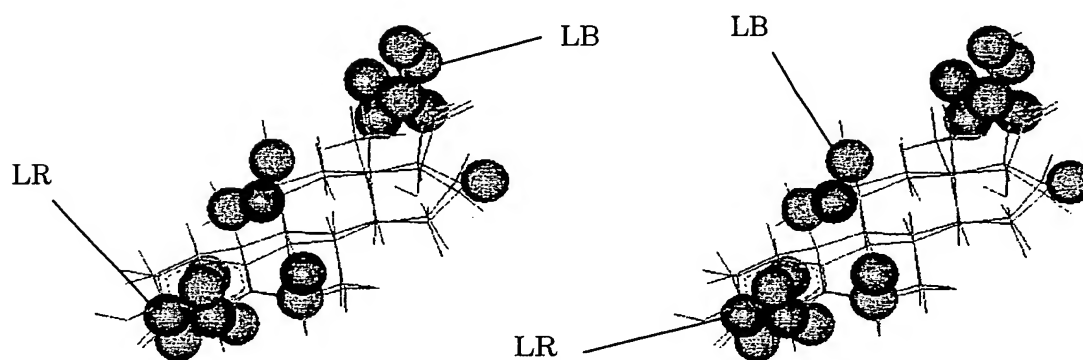


REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.02 OR MORE)

Components 1,  $r^2$ : 0.568,  $q^2$ : 0.381

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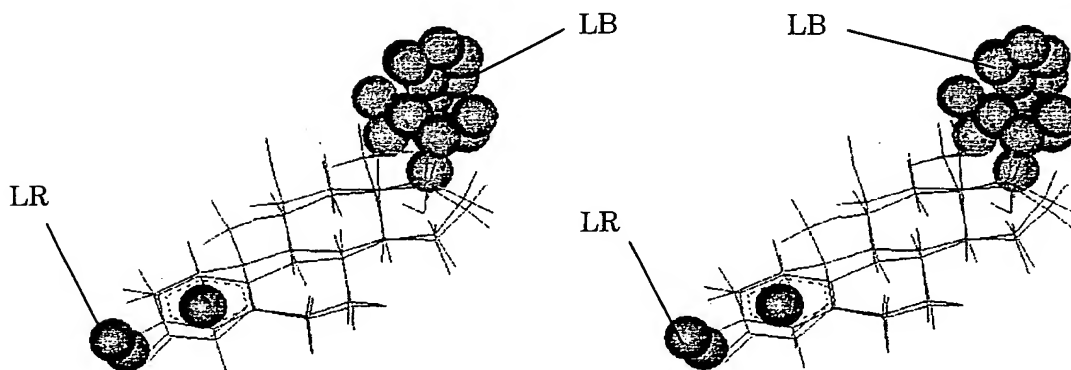
Fig.27



REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.03 OR MORE)

Components 2,  $r^2$ : 0.879,  $q^2$ : 0.707

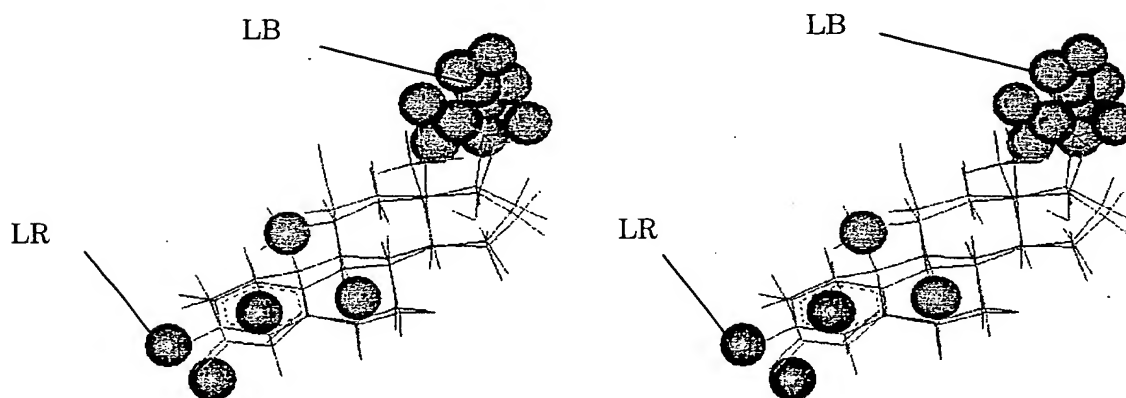
Fig.28



REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.02 OR MORE)

Components 2,  $r^2$ : 0.666,  $q^2$ : 0.408

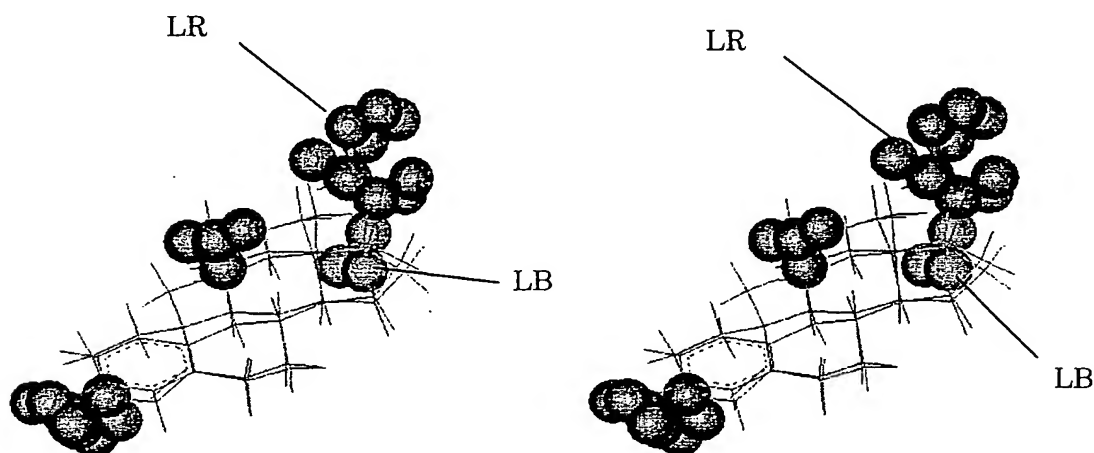
Fig.29



REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.03 OR MORE)

Components 2,  $r^2$ : 0.772,  $q^2$ : 0.442

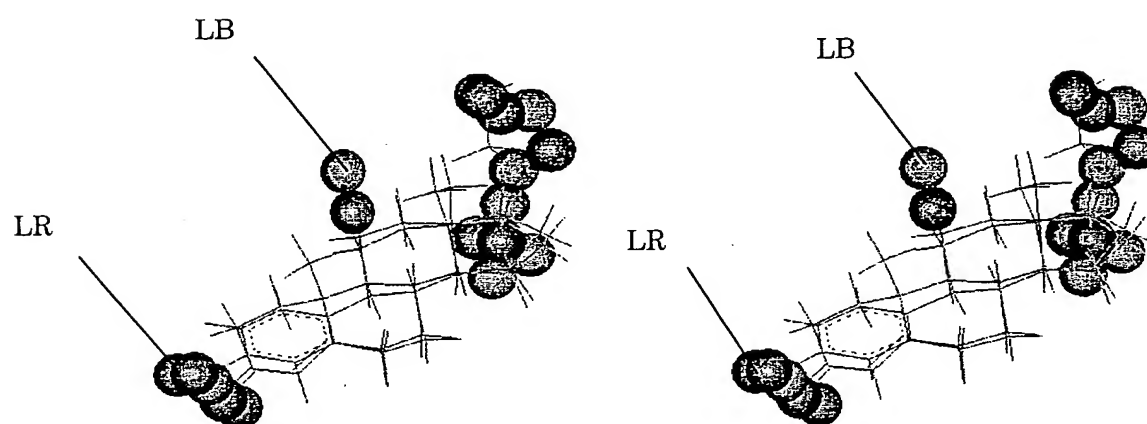
Fig. 30



REGIONS LR (ORANGE) WHERE POSITIVE HASL PARAMETERS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE POSITIVE HASL PARAMETERS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUM  $\times$  STANDARD DEVIATION IS 0.01 OR MORE)

Components 1,  $r^2$ : 0.881,  $q^2$ : 0.747

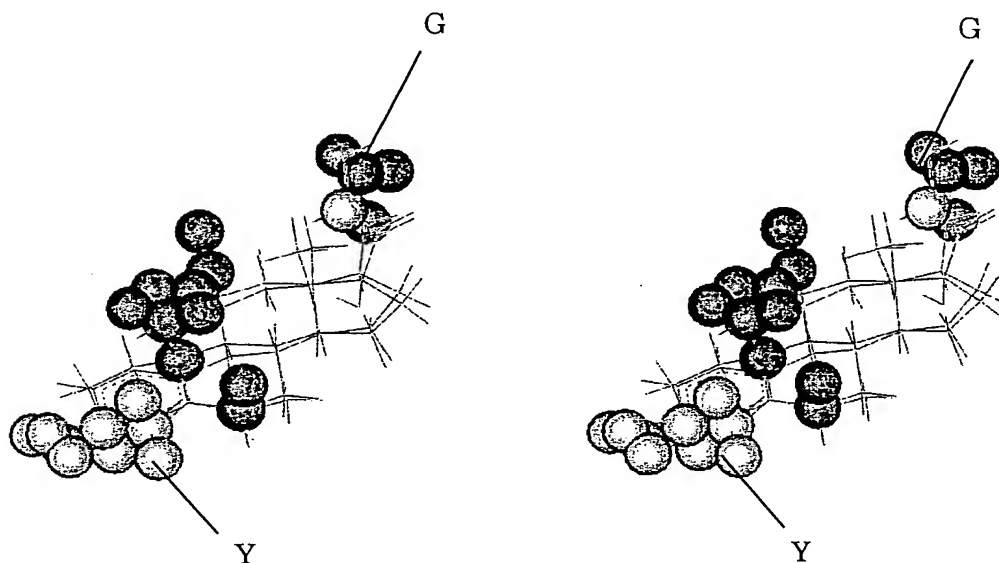
Fig.31



REGIONS LR (ORANGE) WHERE POSITIVE HASL PARAMETERS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE POSITIVE HASL PARAMETERS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.03 OR MORE)

Components 2,  $r^2$ : 0.810,  $q^2$ : 0.534

Fig.32

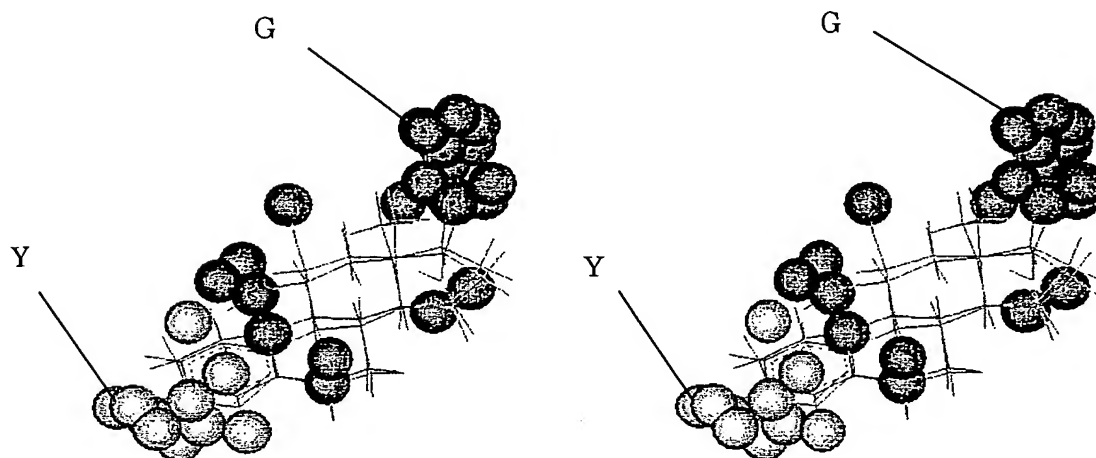


REGIONS G (GREEN) WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
AND REGIONS Y (YELLOW) WHERE ACTIVITY WILL BE WEAKENED STERICALLY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.03 OR MORE)

Components 3,  $r^2$ : 0.847,  $q^2$ : 0.715



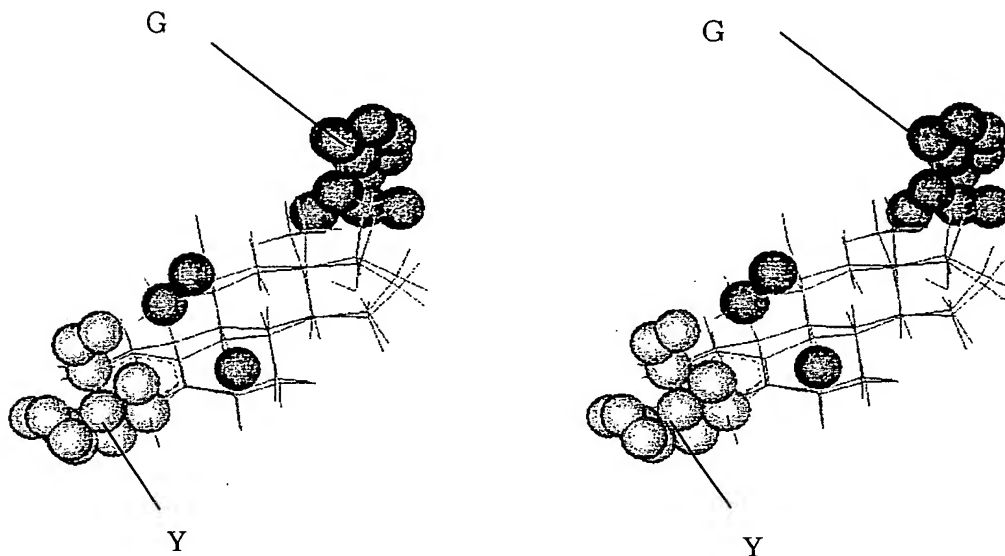
Fig. 33



REGIONS G (GREEN) WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
AND REGIONS Y (YELLOW) WHERE ACTIVITY WILL BE WEAKENED STERICALLY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.01 OR MORE)

Components 2,  $r^2$ : 0.844,  $q^2$ : 0.725

Fig.34

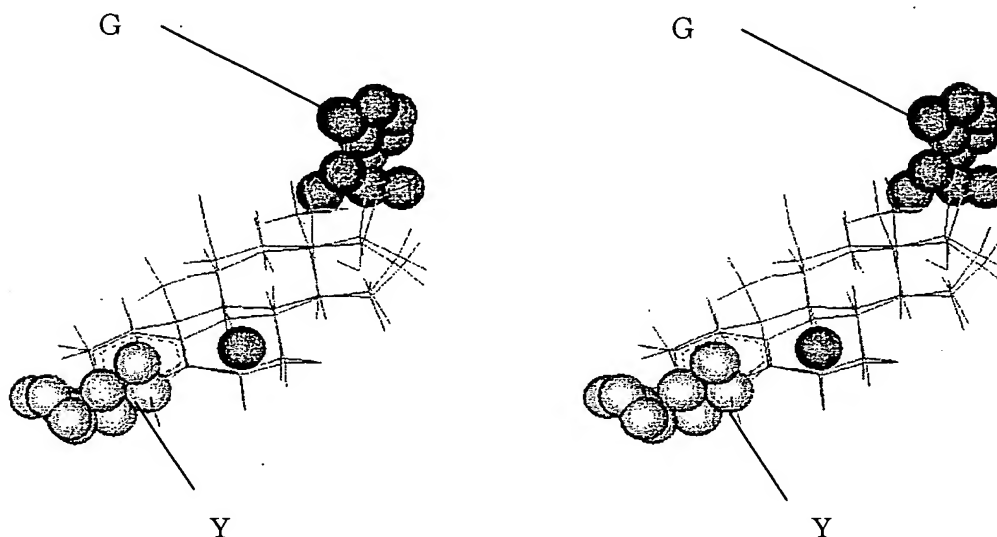


REGIONS G (GREEN) WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
AND REGIONS Y (YELLOW) WHERE ACTIVITY WILL BE WEAKENED STERICALLY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.01 OR MORE)

Components 2,  $r^2$ : 0.797,  $q^2$ : 0.698

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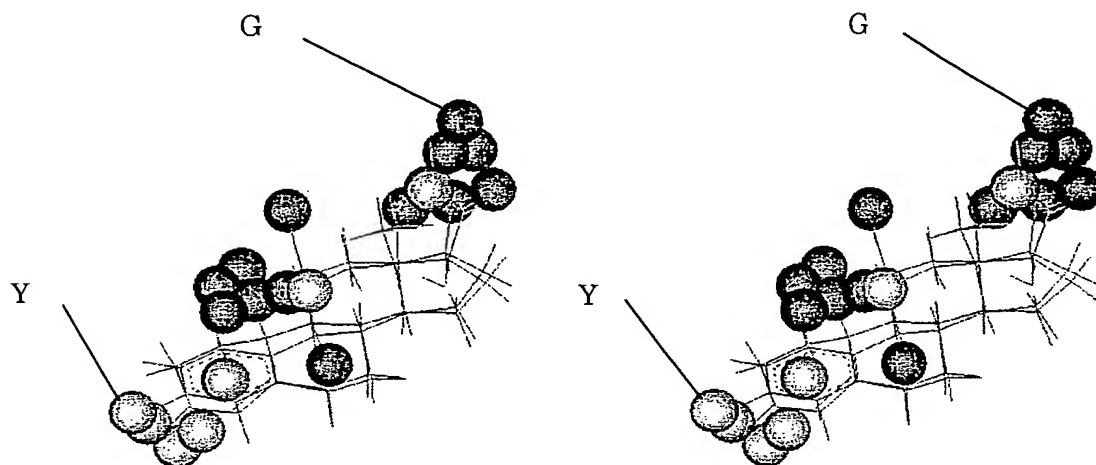
Fig.35



REGIONS G (GREEN) WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
AND REGIONS Y (YELLOW) WHERE ACTIVITY WILL BE WEAKENED STERICALLY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.02 OR MORE)

Components 2,  $r^2$ : 0.781,  $q^2$ : 0.624

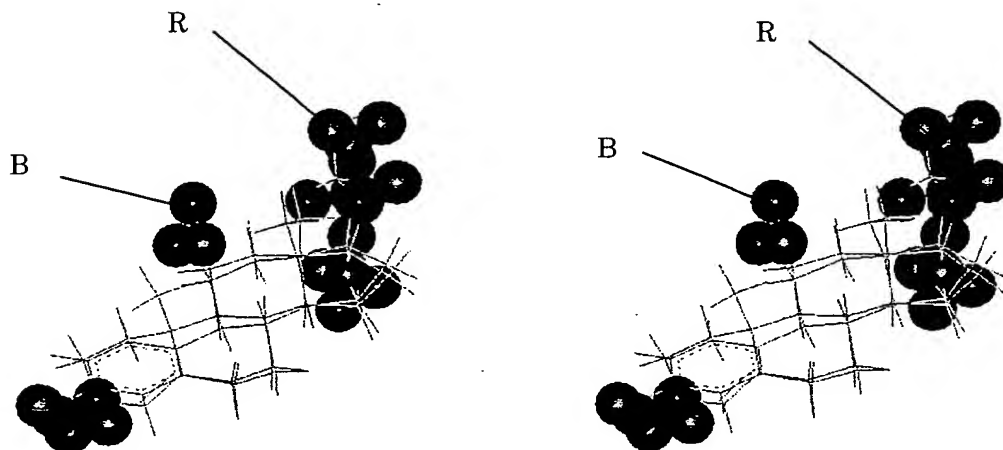
Fig.36



REGIONS G (GREEN) WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
AND REGIONS Y (YELLOW) WHERE ACTIVITY WILL BE WEAKENED STERICALLY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.02 OR MORE)

Components 2,  $r^2$ : 0.902,  $q^2$ : 0.806

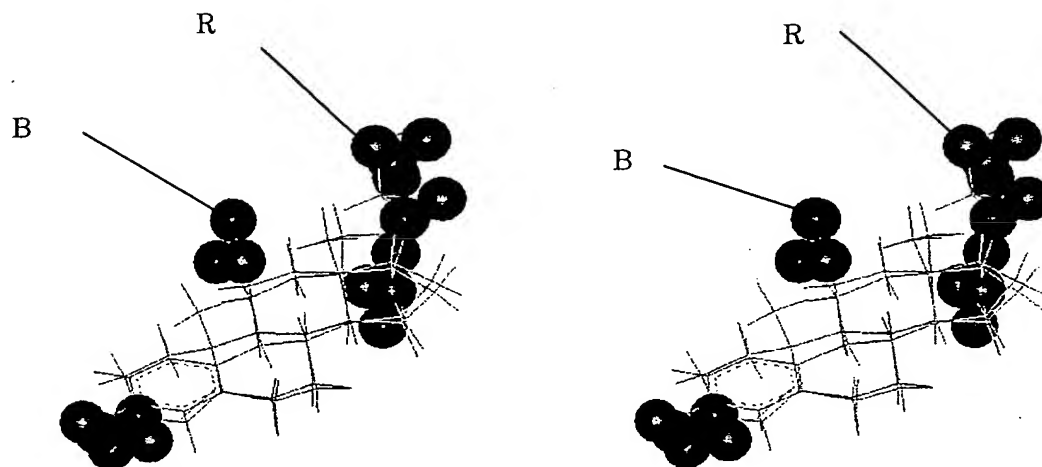
Fig.37



REGIONS B (BLUE) WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
AND REGIONS R (RED) WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.03 OR MORE)

Components 4,  $r^2$ : 0.970,  $q^2$ : 0.761

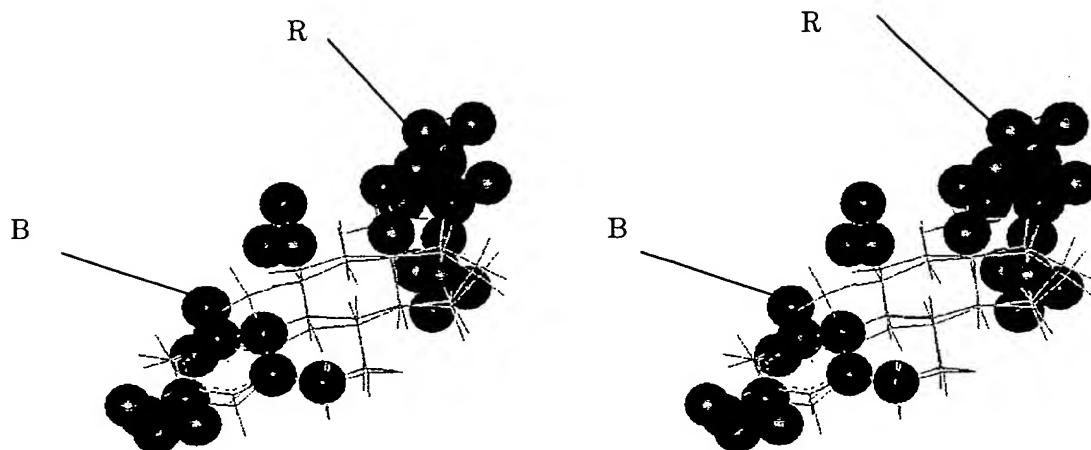
Fig.38



REGIONS B (BLUE) WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
AND REGIONS R (RED) WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.03 OR MORE)

Components 4,  $r^2$ : 0.970,  $q^2$ : 0.776

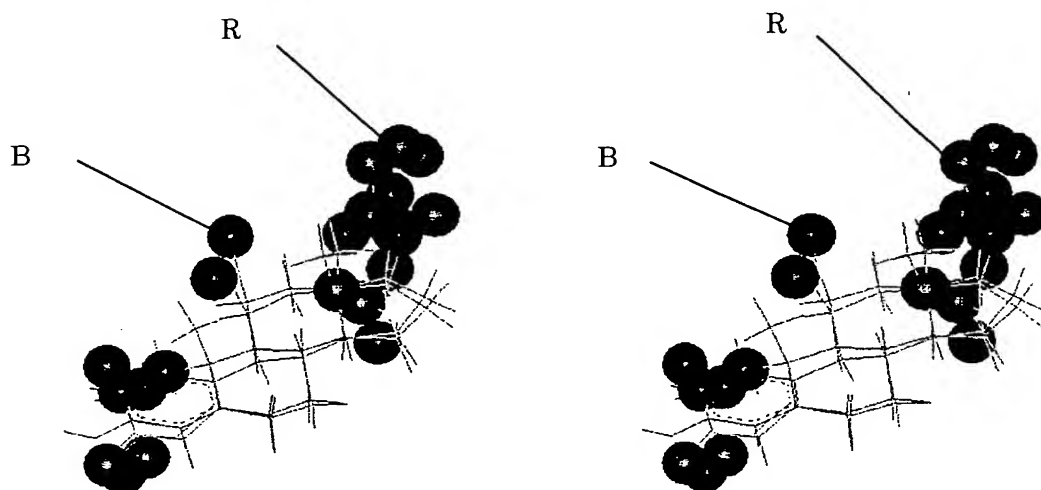
Fig.39



REGIONS B (BLUE) WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
AND REGIONS R (RED) WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.03 OR MORE)

Components 4,  $r^2$ : 0.949,  $q^2$ : 0.586

Fig.40



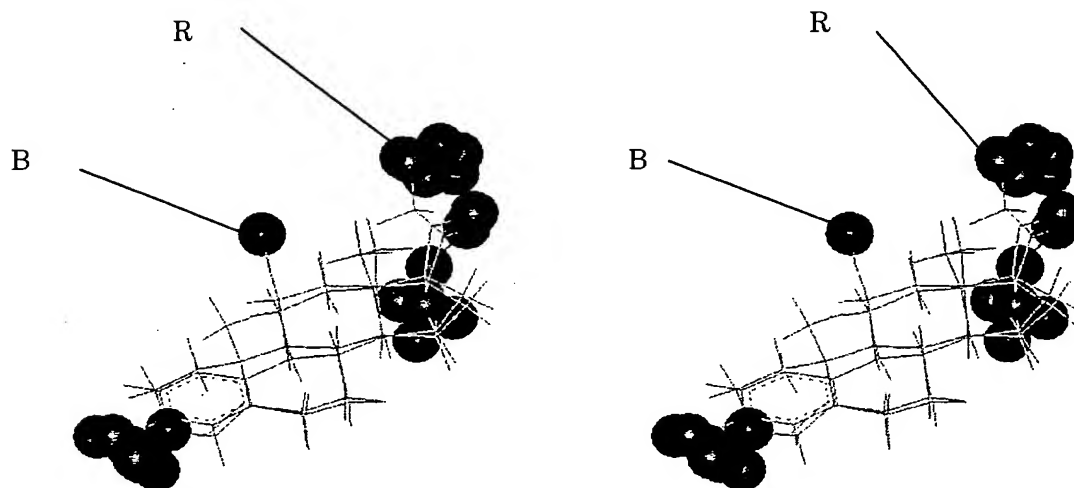
REGIONS B (BLUE) WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
AND REGIONS R (RED) WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.04 OR MORE)

Components 4,  $r^2$ : 0.903,  $q^2$ : 0.579



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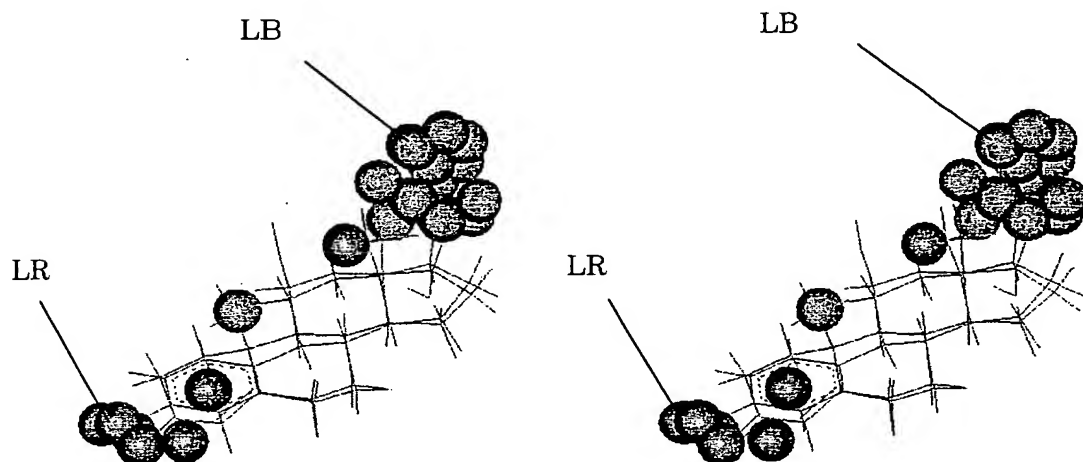
Fig.41



REGIONS B (BLUE) WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
AND REGIONS R (RED) WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.03 OR MORE)

Components 6,  $r^2$ : 0.983,  $q^2$ : 0.719

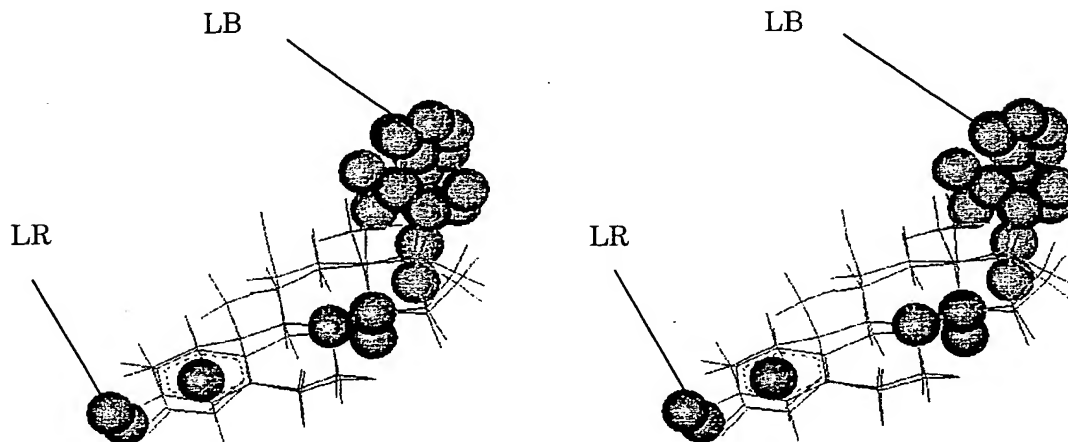
Fig.42



REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.02 OR MORE)

Components 2,  $r^2$ : 0.700,  $q^2$ : 0.254

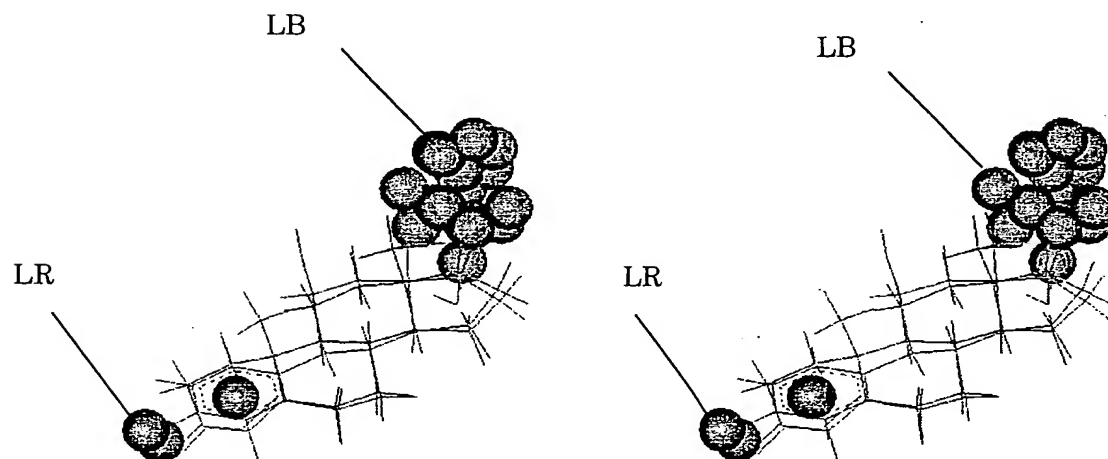
Fig.43



REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.02 OR MORE)

Components 2,  $r^2$ : 0.612,  $q^2$ : 0.171

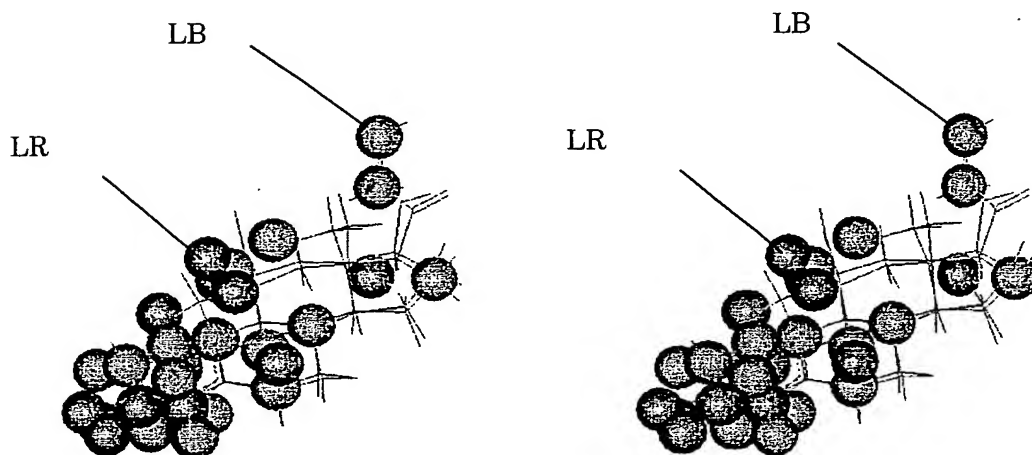
Fig.44



REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.02 OR MORE)

Components 2,  $r^2$ : 0.666,  $q^2$ : 0.408

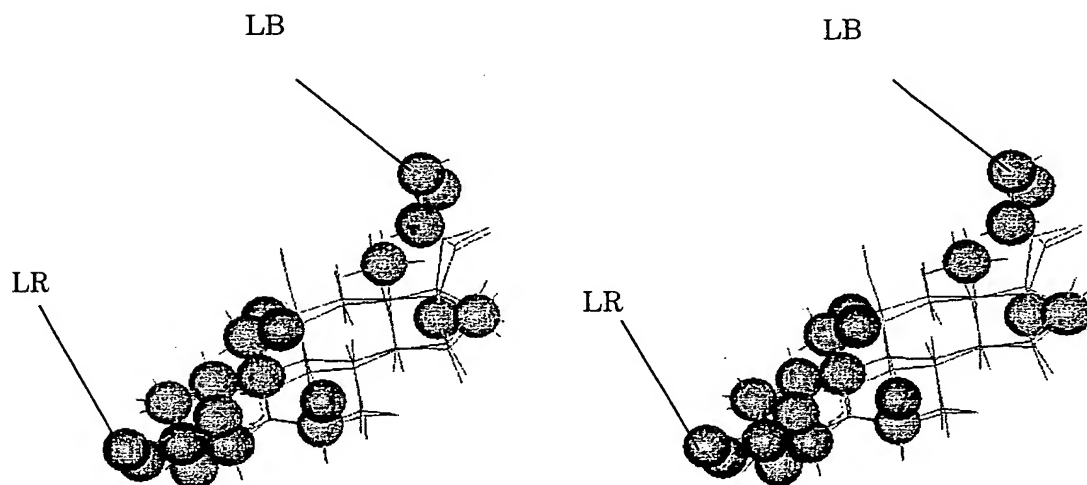
Fig.45



REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.04 OR MORE)

Components 4,  $r^2$ : 0.934,  $q^2$ : 0.705

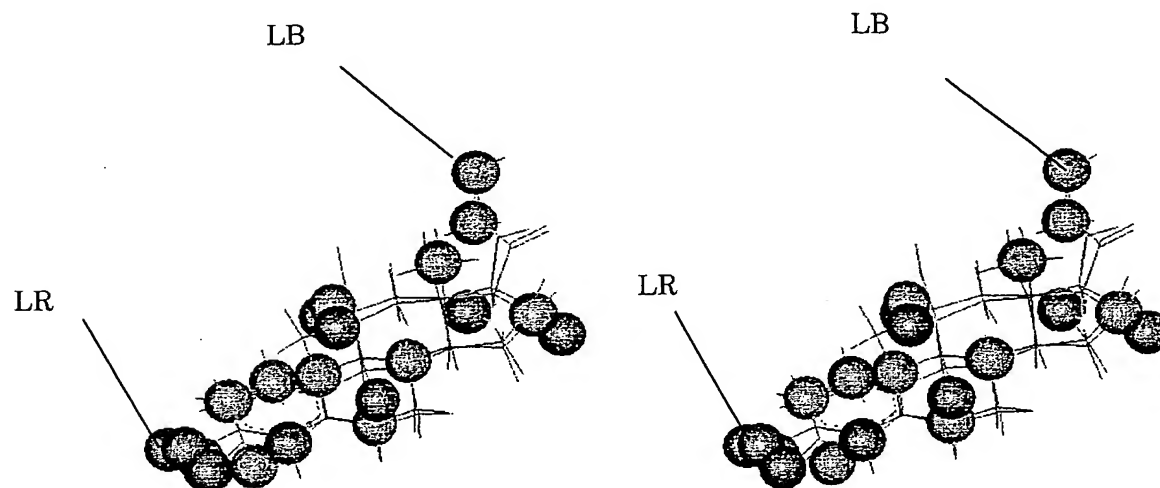
Fig.46



REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.03 OR MORE)

Components 3,  $r^2$ : 0.924,  $q^2$ : 0.741

Fig.47

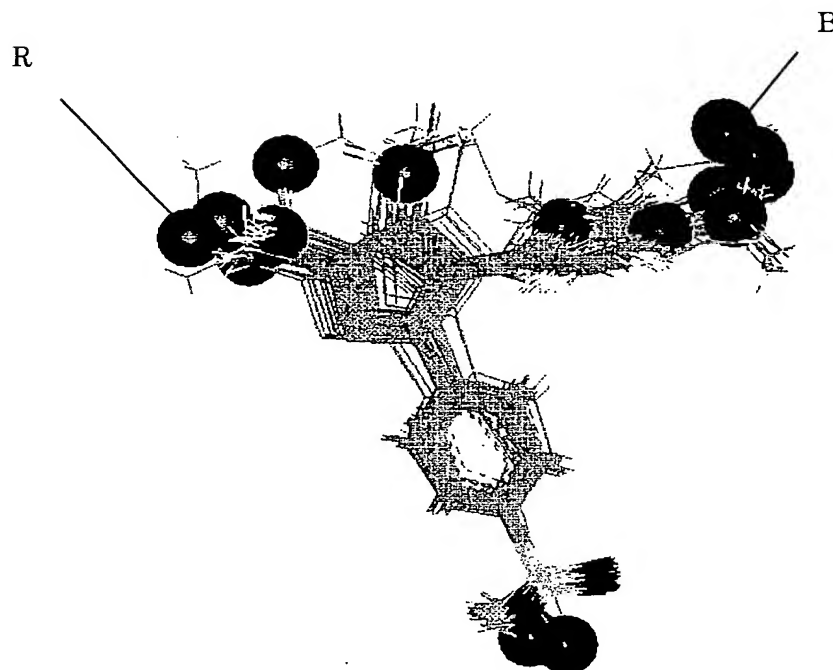


REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.02 OR MORE)

Components 5,  $r^2$ : 0.950,  $q^2$ : 0.744

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Fig.48

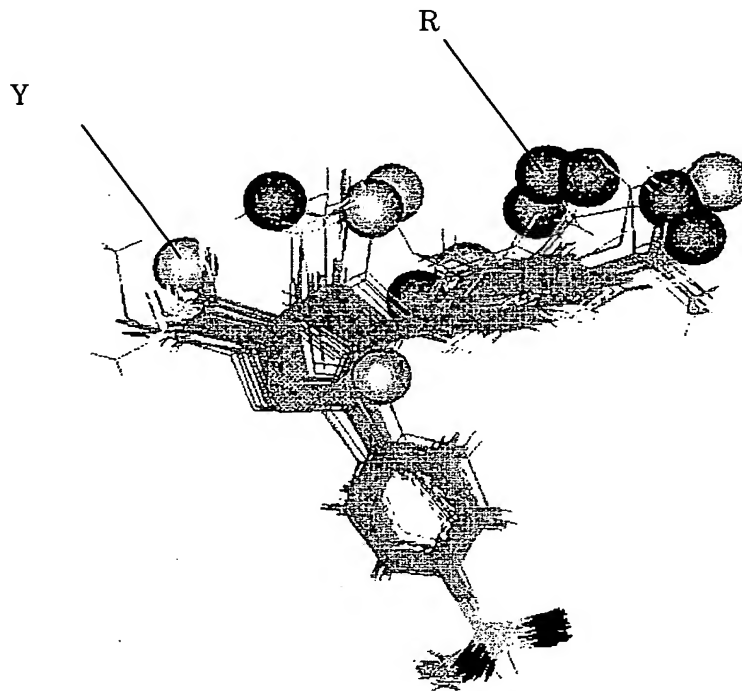


REGIONS B (BLUE) WHERE POSITIVE CHARGES WILL ENHANCE ACTIVITY  
AND REGIONS R (RED) WHERE NEGATIVE CHARGES WILL ENHANCE ACTIVITY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.02 OR MORE)

Components 2,  $r^2$ : 0.796,  $q^2$ : 0.411



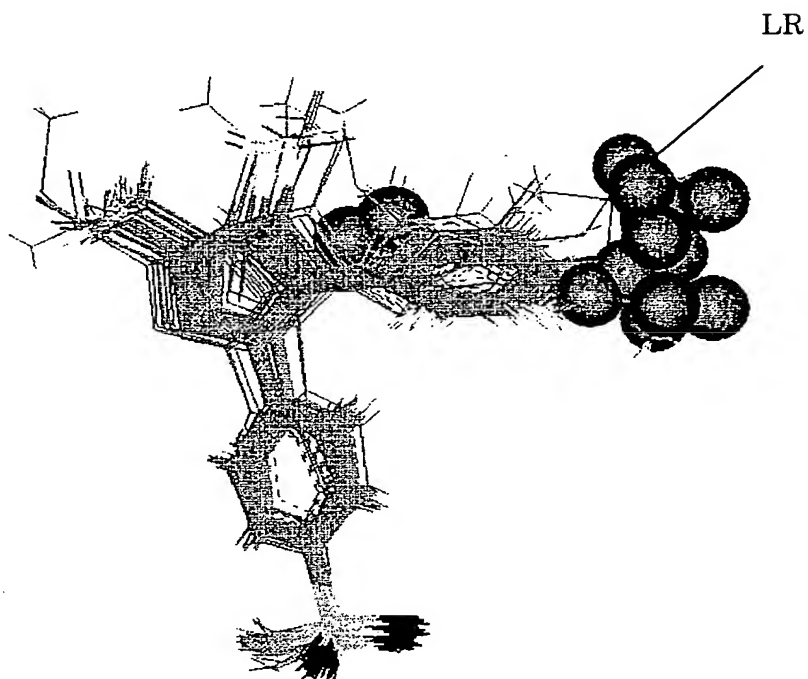
Fig.49



REGIONS G (GREEN) WHERE ACTIVITY WILL BE ENHANCED STERICALLY  
AND REGIONS Y (YELLOW) WHERE ACTIVITY WILL BE WEAKENED STERICALLY  
(REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION  
IS 0.02 OR MORE)

50/50

Fig. 50



REGIONS LR (ORANGE) WHERE HYDROPHOBIC INTERACTIONS WILL ENHANCE ACTIVITY AND REGIONS LB (LIGHT BLUE) WHERE HYDROPHOBIC INTERACTIONS WILL WEAKEN ACTIVITY (REGIONS WHERE COEFFICIENT IN EACH COLUMN  $\times$  STANDARD DEVIATION IS 0.03 OR MORE)

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